

1/25

Parasite donor age (years)

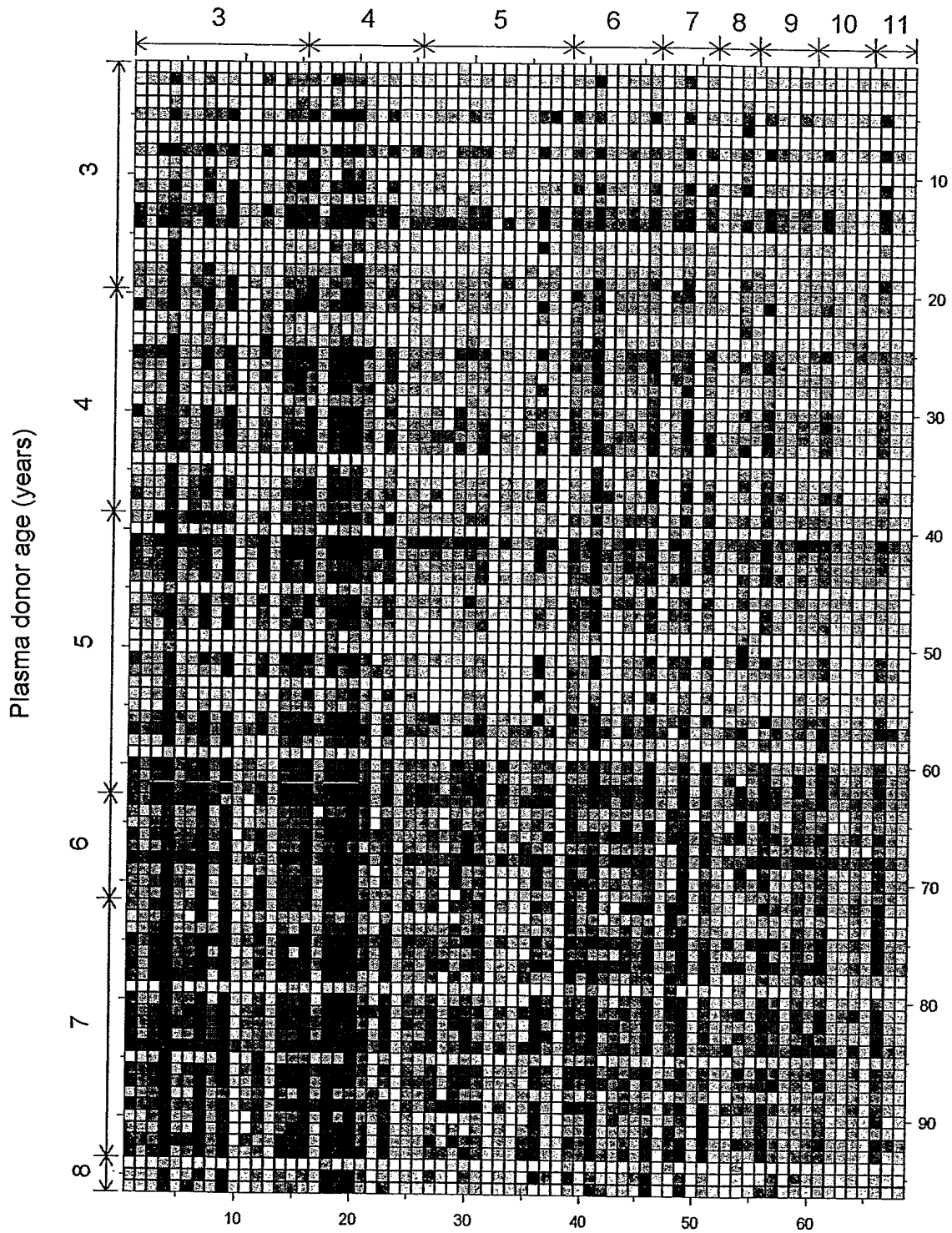


Fig. 1

SUBSTITUTE SHEET (RULE 26)

2/25

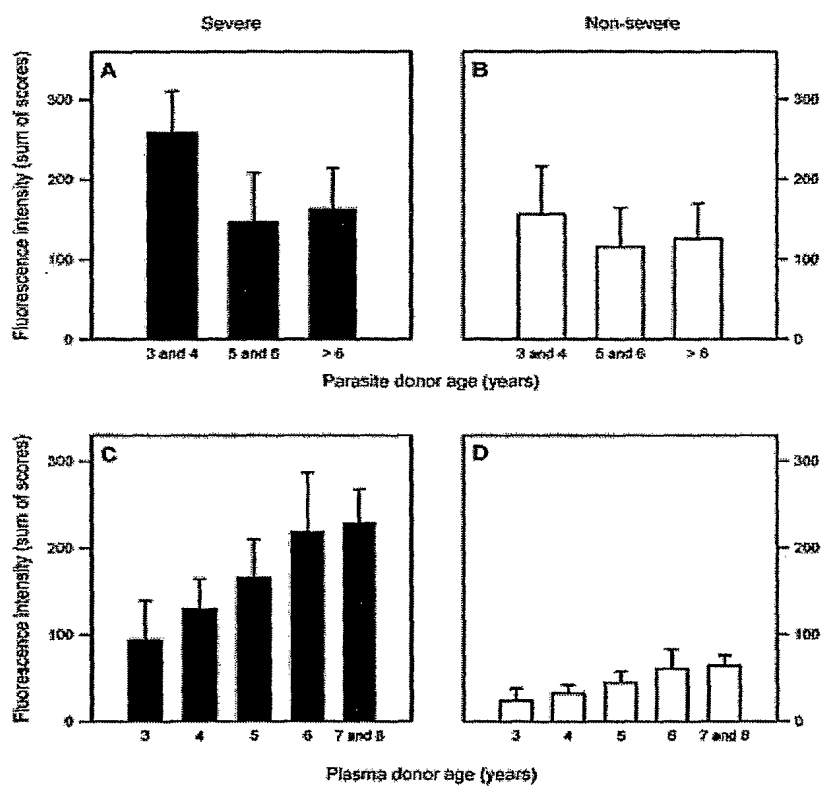
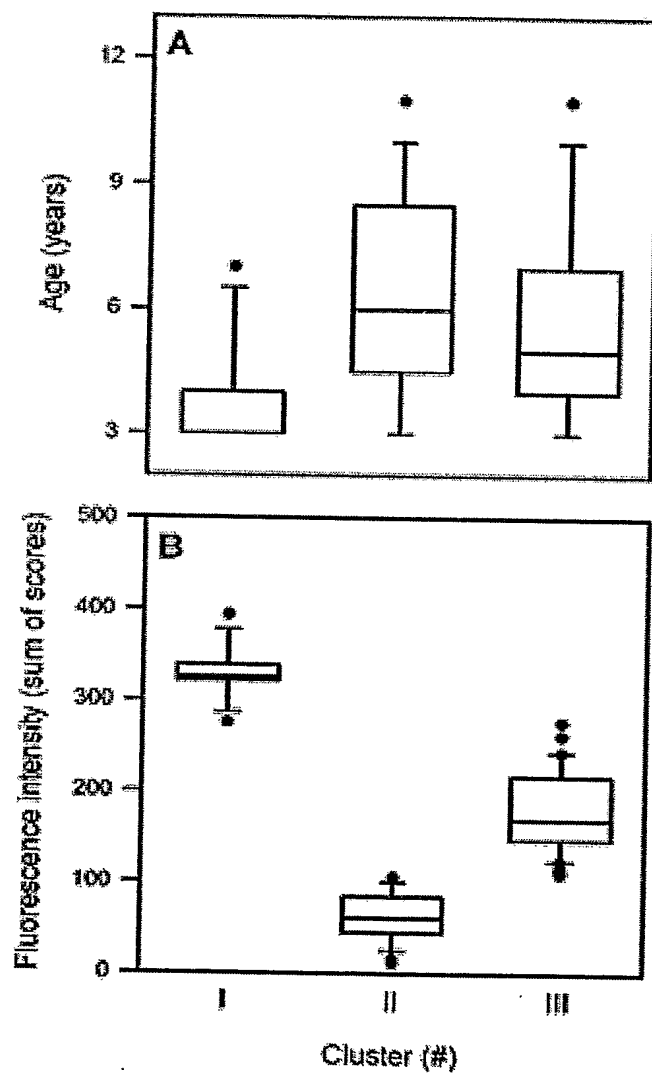


Fig. 2

3/25**Fig. 3**

4/25

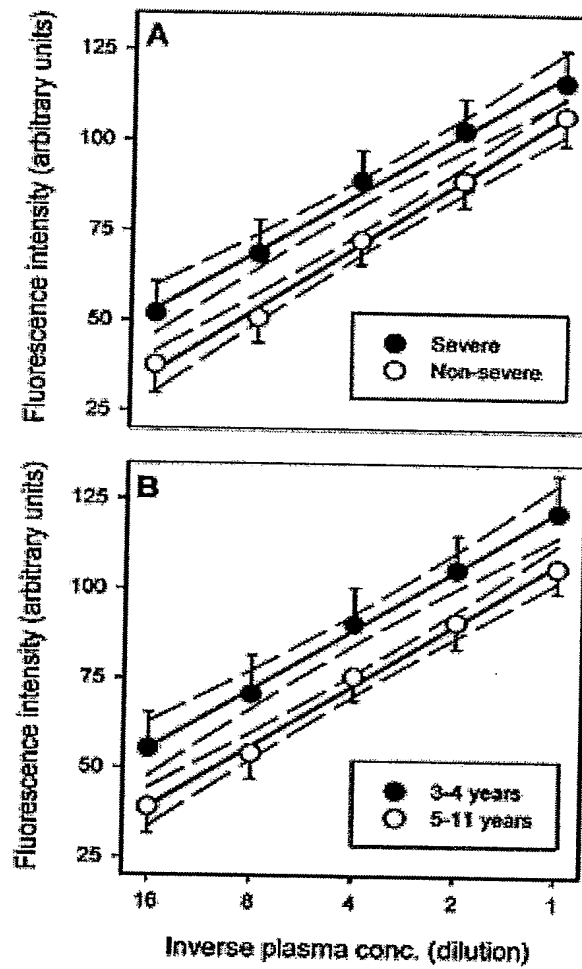


Fig. 4

5/25

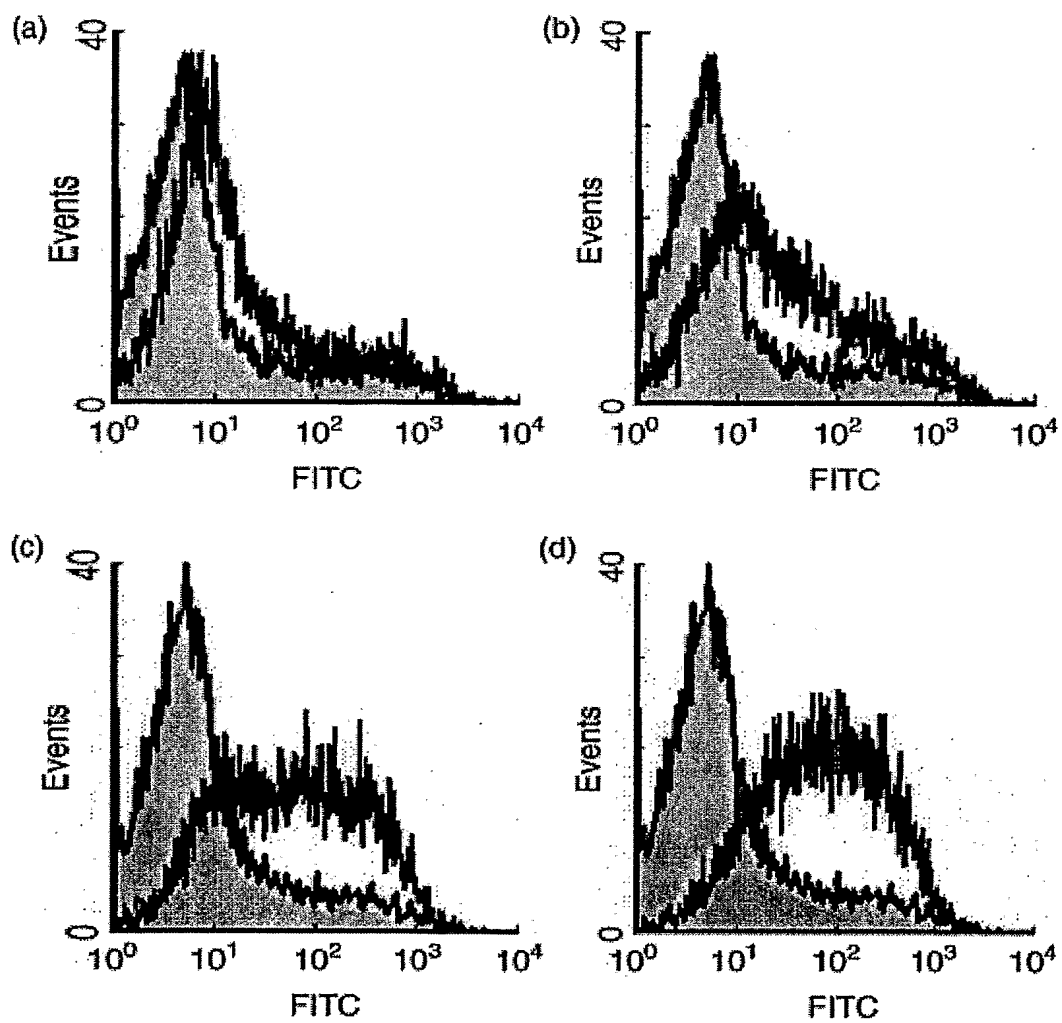


Fig. 5

6/25

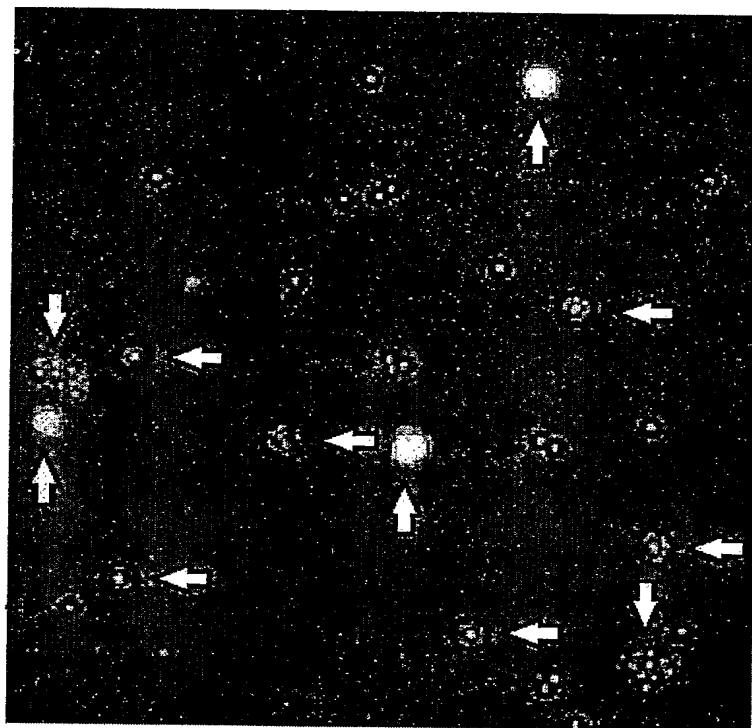


Fig. 6

7/25

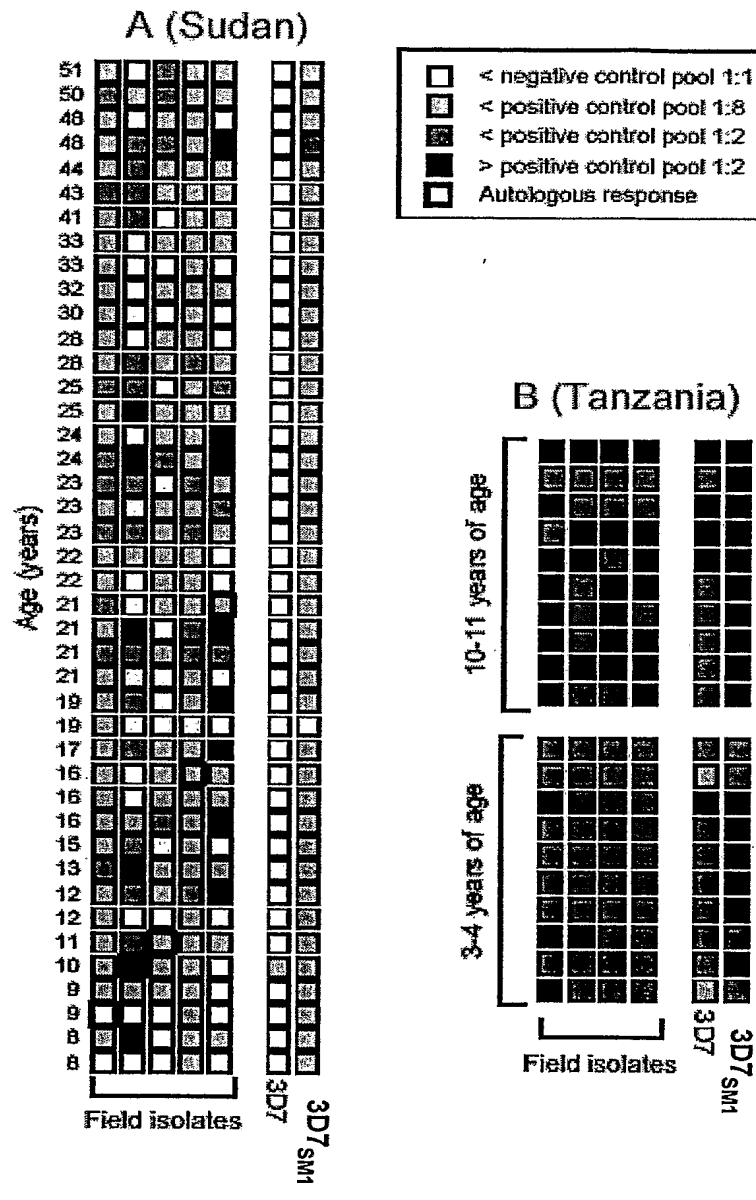
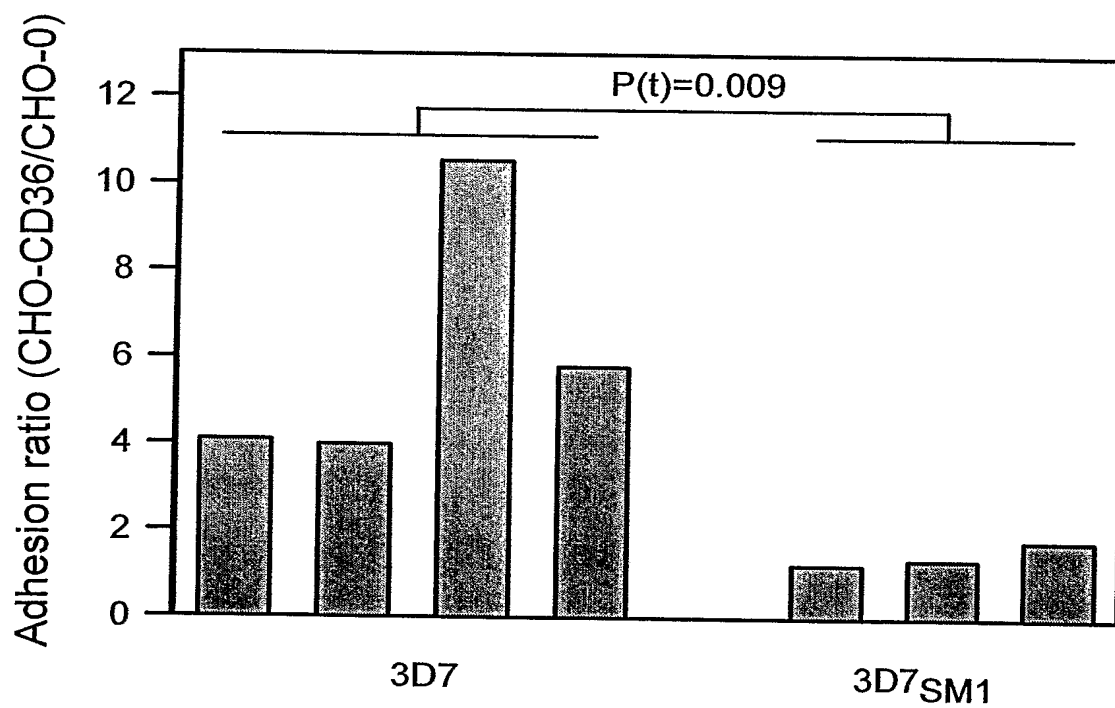


Fig. 7

8/25**Fig. 8**

9/25

var1

var2

var group A

var group B/A

Gene	Location	Orientation		DBL1-		Intron	ATS	3' region	Domain structure									
		(transcribed towards)	5' region	CIDR1	upsD				upsE	upsA	A	None	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- β	C2
PFE1640W**	Telomeric	Telomere	upsD	A	A	None	None	None	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- β	C2	DBL4- γ	DBL5- γ	DBL6- β	DBL7- ϵ ...
PFL0030c	Near telomere	Telomere	upsE	None	None	AI	D	X	DBL1- α	DBL2- β	DBL3- γ	DBL4- δ	DBL5- ϵ	DBL6- ζ	DBL7- η	DBL8- θ	DBL9- ι	DBL10- κ
PFD1235W	Near telomere	Telomere	upsA	A	A	AI	A	A	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- β	C2	DBL4- γ	DBL5- γ	DBL6- β	DBL7- ϵ ...
MAL7P1.1	Telomeric	Telomere	upsA	A	A	AI	A	A	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- β	C2	DBL4- γ	DBL5- γ	DBL6- β	DBL7- ϵ ...
PF11_0521	Telomeric	Telomere	upsA	A	A	AI	A	A	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- β	C2	DBL4- γ	DBL5- γ	DBL6- β	DBL7- ϵ ...
PF13_0003	Near telomere	Telomere	upsA	A	A	AI	A	A	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- β	C2	DBL4- γ	DBL5- γ	DBL6- β	DBL7- ϵ ...
PF08_0141	Near telomere	Telomere	upsA	A	X	A	A	A	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- β	C2	DBL4- γ	DBL5- γ	DBL6- β	DBL7- ϵ ...
PF11_0008	Near telomere	Telomere	upsA	A	X	A	A	A	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- β	C2	DBL4- γ	DBL5- γ	DBL6- β	DBL7- ϵ ...
PFD0020c	Near telomere	Telomere	upsA	A	X	A	A	A	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- β	C2	DBL4- γ	DBL5- γ	DBL6- β	DBL7- ϵ ...
PFA0015c	Near telomere	Telomere	upsA	A*	AI	A	A	A	DBL1- α	DBL2- ϵ	ATS							
MAL6P1.314	Near telomere	Telomere	upsA	A*	AI	A	A	A	DBL1- α	DBL2- ϵ	ATS							
PF1820W	Near telomere	Telomere	upsA	A*	AI	A	A	A	DBL1- α	DBL2- ϵ	ATS							
PF08_0140	Near telomere	Centromere	upsBsh	A	B	B	B	B	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- β	C2	DBL4- γ	DBL5- γ	DBL6- β	DBL7- ϵ ...
MAL6P1.316	Near telomere	Centromere	upsBsh^1	A	X	X	X	X	DBL1- α	CIDR- β	DBL2- β	C2	DBL3- γ	DBL4- ζ	DBL5- ϵ	ATS		
PFL0020w	Near telomere	Centromere	upsBsh	X	X	X	X	B	DBL1- α	CIDR- β	DBL2- β	C2	DBL3- γ	DBL4- ζ	DBL5- ϵ	ATS		
MAL6P1.4	Telomeric	Centromere	upsB	C	X	X	X	B	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- γ	DBL4- δ	CIDR- γ	DBL5- ϵ	DBL6- ζ	DBL7- η ...
PF11_0007	Telomeric	Centromere	upsB	X	B	B	B	D	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- β	C2	DBL4- γ	DBL5- γ	DBL6- β	DBL7- ϵ ...
PF08_0142	Telomeric	Centromere	upsB	B	B	B	B	D	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- β	C2	DBL4- γ	DBL5- γ	DBL6- β	DBL7- ϵ ...
PFE0005W	Telomeric	Centromere	upsB	B	B	B	B	D	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- β	C2	DBL4- γ	DBL5- γ	DBL6- β	DBL7- ϵ ...
PFA0005W	Telomeric	Centromere	upsB	B	B	B	C	B	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- β	C2	DBL4- γ	DBL5- γ	DBL6- β	DBL7- ϵ ...
PFA0765c	Telomeric	Centromere	upsB	B	B	B	B	B	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- β	C2	DBL4- γ	DBL5- γ	DBL6- β	DBL7- ϵ ...
PFC1120c	Telomeric	Centromere	upsB	B	B	B	B	B	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- β	C2	DBL4- γ	DBL5- γ	DBL6- β	DBL7- ϵ ...
PFD0005W	Telomeric	Centromere	upsB	B	B	B	B	B	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- β	C2	DBL4- γ	DBL5- γ	DBL6- β	DBL7- ϵ ...
PF0005W	Telomeric	Centromere	upsB	D	B	B	B	B	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- β	C2	DBL4- γ	DBL5- γ	DBL6- β	DBL7- ϵ ...
PF13_0364	Telomeric	Centromere	upsB	D	B	B	B	B	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- β	C2	DBL4- γ	DBL5- γ	DBL6- β	DBL7- ϵ ...
PF07_0139	Telomeric	Centromere	upsB	D	X	B	B	B	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- β	C2	DBL4- γ	DBL5- γ	DBL6- β	DBL7- ϵ ...
PFB1055c	Telomeric	Centromere	upsB	D	X	B	B	B	DBL1- α	CIDR1- α	DBL2- β	C2	DBL3- β	C2	DBL4- γ	DBL5- γ	DBL6- β	DBL7- ϵ ...

Fig. 9

SUBSTITUTE SHEET (RULE 26)

10/25

var group B												
PF10_0406	Telomeric	Centromere	upsB	B	X	B	B	DBL1- α	CIDR1- α	DBL2- δ	CIDR- β	ATS
PFL0005W	Telomeric	Centromere	upsB	B	X	B	B	DBL1- α	CIDR1- α	DBL2- δ	CIDR- β	ATS
PFE0010W	Telomeric	Centromere	upsB	B	X	B	B	DBL1- α	CIDR1 α	DBL2- γ	ATS	
PFC0005W	Telomeric	Centromere	upsB	B	X	B	B	DBL1- α	CIDR1- α	DBL2- δ	CIDR- β	ATS
PFL2665c	Telomeric	Centromere	upsB	B	X	B	B	DBL1- α	CIDR1- α	DBL2- δ	CIDR- β	ATS
PF13_0001	Telomeric	Centromere	upsB	B	X	B	B	DBL1- α	CIDR1- α	DBL2- δ	CIDR- β	ATS
MAL6P1.1	Telomeric	Centromere	upsB	E	B	B	B	DBL1- α	CIDR1- α	DBL2- δ	CIDR- β	ATS
PFD1245c	Telomeric	Centromere	upsB	X	X	C	B	DBL1- α	CIDR1- α	DBL2- δ	CIDR- β	ATS
PF11830c	Telomeric	Centromere	upsB	C	X	B	B	DBL1- α	CIDR1- α	DBL2- δ	CIDR- γ	ATS
PF10_0001	Telomeric	Centromere	upsB	C	X	B	B	DBL1- α	CIDR1- α	DBL2- δ	CIDR- γ	ATS
PFL0935c	Centromeric	Telomere	upsB	D	X	C	B	DBL1- α	CIDR1- α	DBL2- δ	CIDR- γ	ATS
PFD0635c	Centromeric	Telomere	upsBsh	C	B	C	C	DBL1- α	CIDR1- α	DBL2- δ	CIDR- γ	ATS
PFL1955W	Centromeric	Telomere	upsBsh	C	B	C	C	DBL1- α	CIDR1- α	DBL2- δ	CIDR- β	ATS
PF08_0106	Centromeric	Telomere	upsBsh	C	B	C	X	DBL1- α	CIDR1- α	DBL2- δ	CIDR- β	ATS
MAL7P1.50	Centromeric	Telomere	upsBsh	C	X	C	X	DBL1- α	CIDR1- α	DBL2- δ	CIDR- γ	ATS
PF08_0103	Centromeric	Telomere	upsBsh	B	X	C	X	DBL1- α	CIDR1- α	DBL2- δ	CIDR- β	ATS
MAL7P1.55	Centromeric	Telomere	upsBsh	B	X	C	C	DBL1- α	CIDR1- α	DBL2- δ	CIDR- γ	ATS
PF07_0050	Centromeric	Telomere	upsBsh	B	AI	B	D	DBL1- α	CIDR1- α	DBL2- δ	C2	DBL3- γ ATS
PFD1005c	Centromeric	Telomere	upsBsh	E	B	B	C	DBL1- α	CIDR1- α	DBL2- δ	CIDR- γ	ATS
PFL1950W	Centromeric	Telomere	upsB ^A	E	X	B	D	DBL1- α	CIDR1- α	DBL2- δ	C2	DBL3- δ CIDR- β ATS
MAL6P1.252	Centromeric	Telomere	upsC	B	B	D	X	DBL1- α	CIDR1- α	DBL2- δ	C2	DBL3- δ CIDR- β ATS
PFD0935c	Centromeric	Telomere	upsC	C	X	D	X	DBL1- α	CIDR1- α	DBL2- δ	CIDR- γ	ATS
MAL7P1.56	Centromeric	Telomere	upsC	C	X	B	D	DBL1- α	CIDR1- α	DBL2- δ	CIDR- β	ATS
PF08_0107	Centromeric	Telomere	upsC	X	B	B	D	DBL1- α	CIDR1- α	DBL2- δ	CIDR- γ	ATS
PF07_0049	Centromeric	Telomere	upsC	C	B	C	X	DBL1- α	CIDR1- α	DBL2- δ	CIDR- γ	ATS
PFD0630c	Centromeric	Telomere	upsC	C	B	C	C	DBL1- α	CIDR1- α	DBL2- δ	CIDR- γ	ATS
PFD1000c	Centromeric	Telomere	upsC	C	B	B	C	DBL1- α	CIDR1- α	DBL2- δ	CIDR- γ	ATS
PFD1015c	Centromeric	Telomere	upsC	D	B	B	X	DBL1- α	CIDR1- α	DBL2- δ	CIDR- β	ATS
PFD0615c	Centromeric	Telomere	upsC	C	X	X	X	DBL1- α	CIDR1- α	DBL2- δ	CIDR- β	ATS
PF07_0051	Centromeric	Telomere	upsC	C	AI	D	X	DBL1- α	CIDR1- α	DBL2- δ	CIDR- β	ATS
PF07_0048	Centromeric	Telomere	upsC	C	X	C	C	DBL1- α	CIDR1- α	DBL2- δ	CIDR- β	ATS
PFL1960W	Centromeric	Telomere	upsC	C	X	C	X	DBL1- α	CIDR1- α	DBL2- δ	CIDR- β	ATS
PFD0625c	Centromeric	Telomere	upsC	C	X	C	X	DBL1- α	CIDR1- α	DBL2- δ	CIDR- β	ATS
var group B/C												
var group C												

Fig. 9 continued a

11/25

B	3D7 gene with closest related 5' sequence				DBL1- 5' region CIDR1 Intron ATS 3' region				Known domain structure
	Strain	sequence							
PEMP1									
var1 family	3D7 homologue: PFE1640w								Both 5' region and coding sequences are conserved [42]
var2 family	3D7 homologue: PFL0030c								Both 5' region and coding sequences are conserved [35]
AAA75397	FOR3	MAL6P1.316	upsBsh ^A	A	nd.	C	D	DBL1- α CIDR1- α DBL2- β C2 DBL3- γ DBL4- δ CIDR- β ATS	
AAA75396	Dd2	PF07_0050	upsB	C	nd.	B	X	DBL1- α CIDR1- α DBL2- β C2 DBL3- γ DBL4- δ CIDR- β ATS	
AAA75398	FOR3	PF07_0139	upsB	E	nd.	B	X	DBL1- α CIDR1- α DBL2- β C2 DBL3- δ CIDR- β ATS	
AAD03351	It	PFL2665c	upsB	X	nd.	nd.	nd.	DBL1- α CIDR1- α DBL2- β C2 DBL3- δ CIDR- β DBL4- γ DBL5- β	
AF193424	It	PF08_0142	upsB	X	nd.	nd.	nd.	DBL1- α CIDR1- α DBL2- β C2 DBL3- γ	
AAB60251	MC	-	nd.	B	nd.	B	D	DBL1- α CIDR1- α DBL2- δ CIDR- γ DBL3- β DBL4- ϵ ATS	
AAC05220	-	PFD0005w	upsB	B	nd.	nd.	nd.	DBL1- α CIDR1- α DBL2- β C2 DBL3- δ	
AAC47438	FCR3	PFB1055c	upsB	X	nd.	B	nd.	DBL1- α CIDR1- α DBL2- β C2 DBL3- δ CIDR- β ATS	
AAB06961	It	PFL0020w	upsBsh	X	nd.	nd.	nd.	DBL1- α CIDR1- α DBL2- β C2 DBL3- δ CIDR- β	
AAA75399	Dd2	PFD1015c	upsC	B	nd.	C	X	DBL1- α CIDR1- α DBL2- δ CIDR- β ATS	
AAC05730	FCR3	-	nd.	C	nd.	C	nd.	DBL1- α CIDR1- α DBL2- δ CIDR- β ATS	

Fig. 9 continued b

12/25

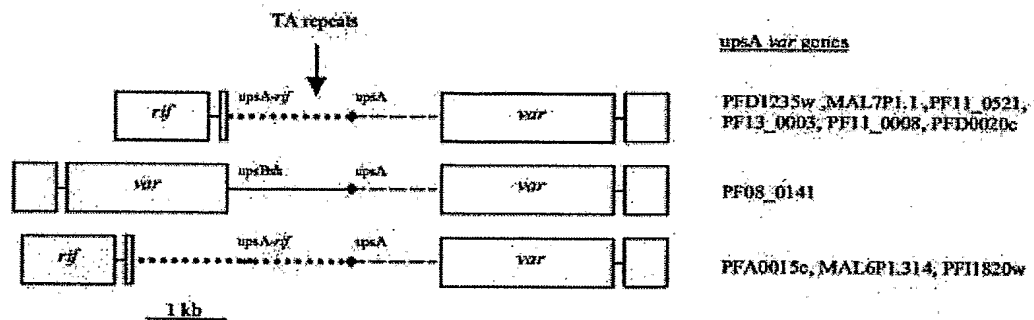


Fig. 10

13 / 25

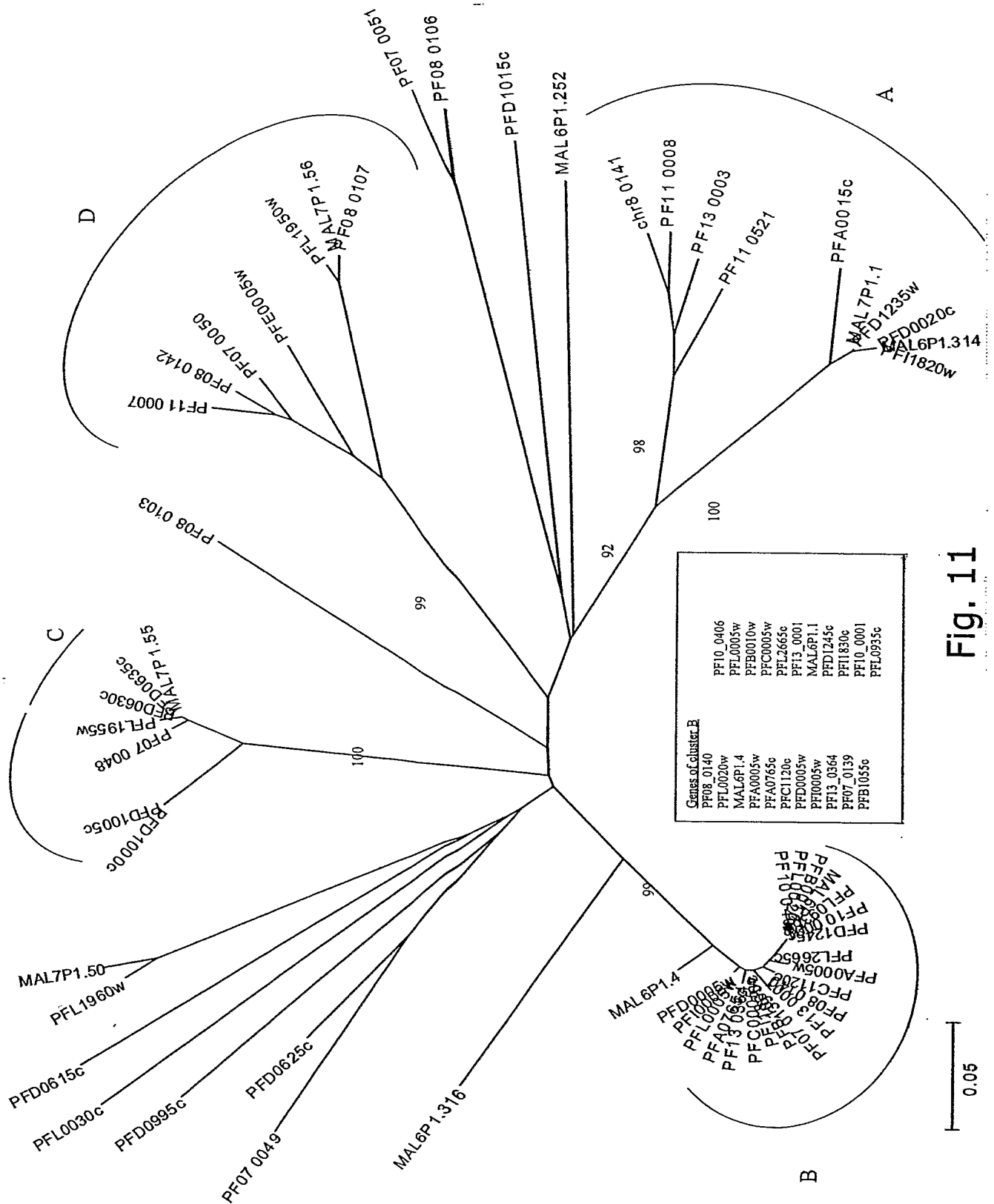
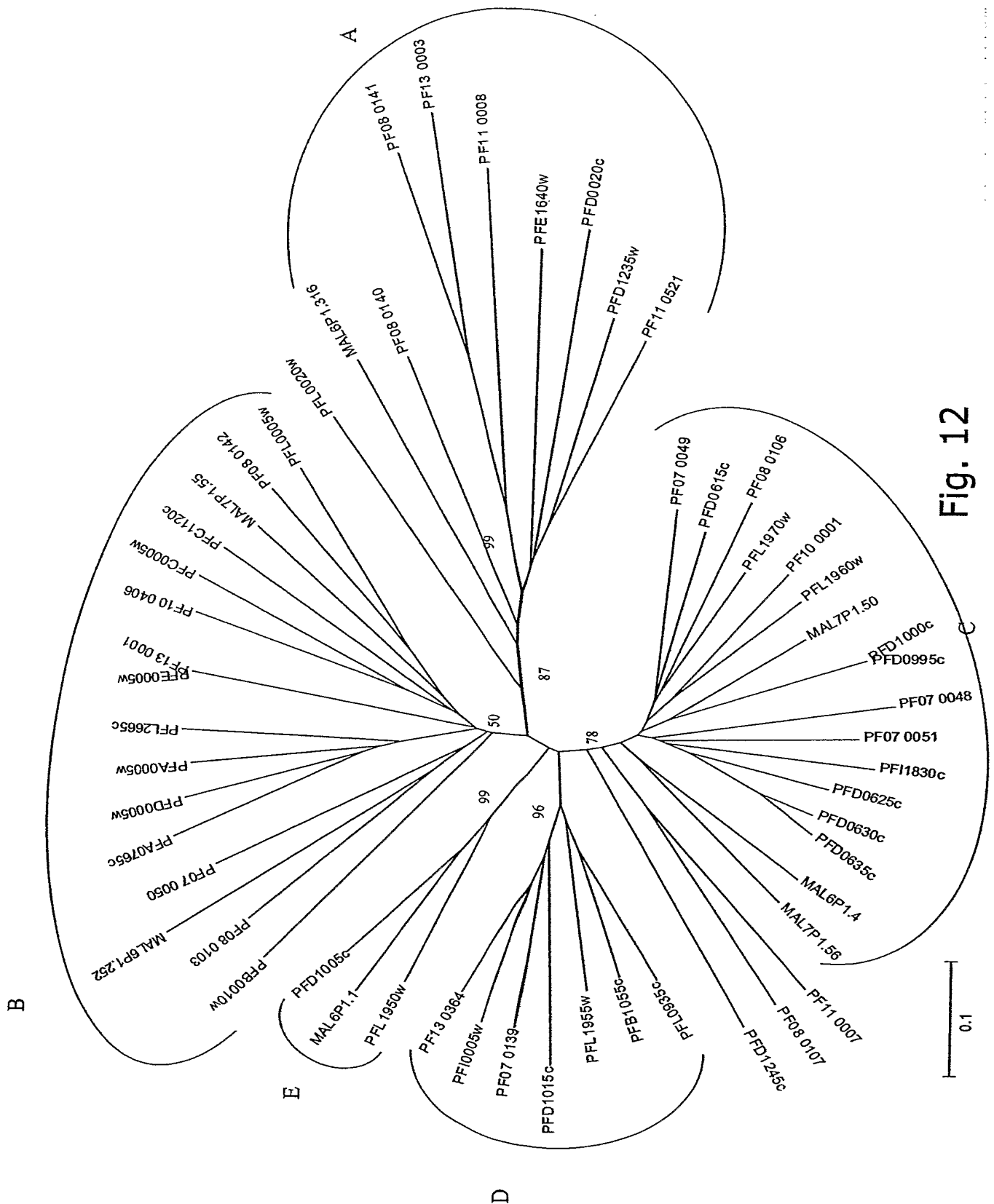


Fig. 11

14/25



15/25

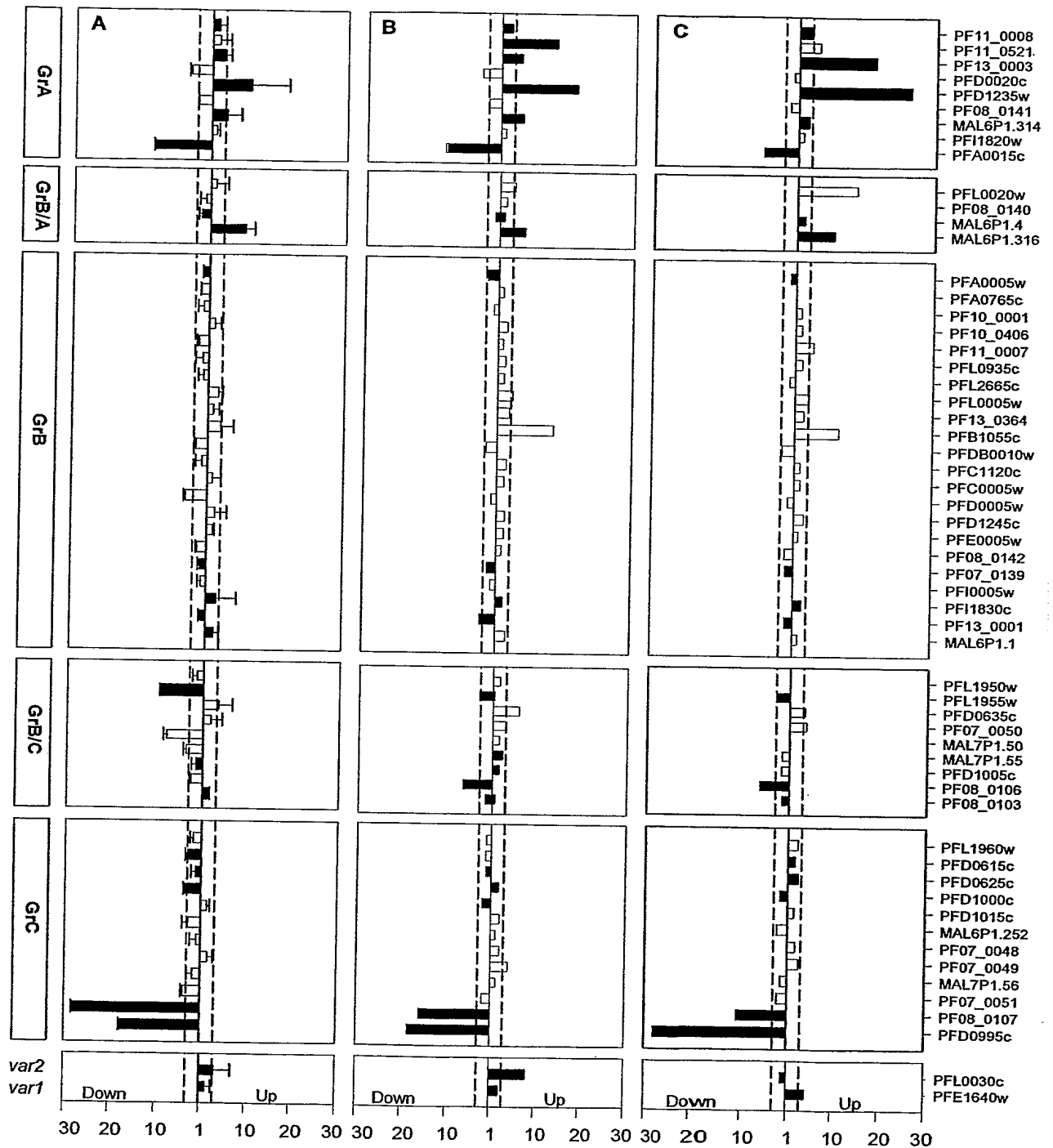


Fig. 13

16/25

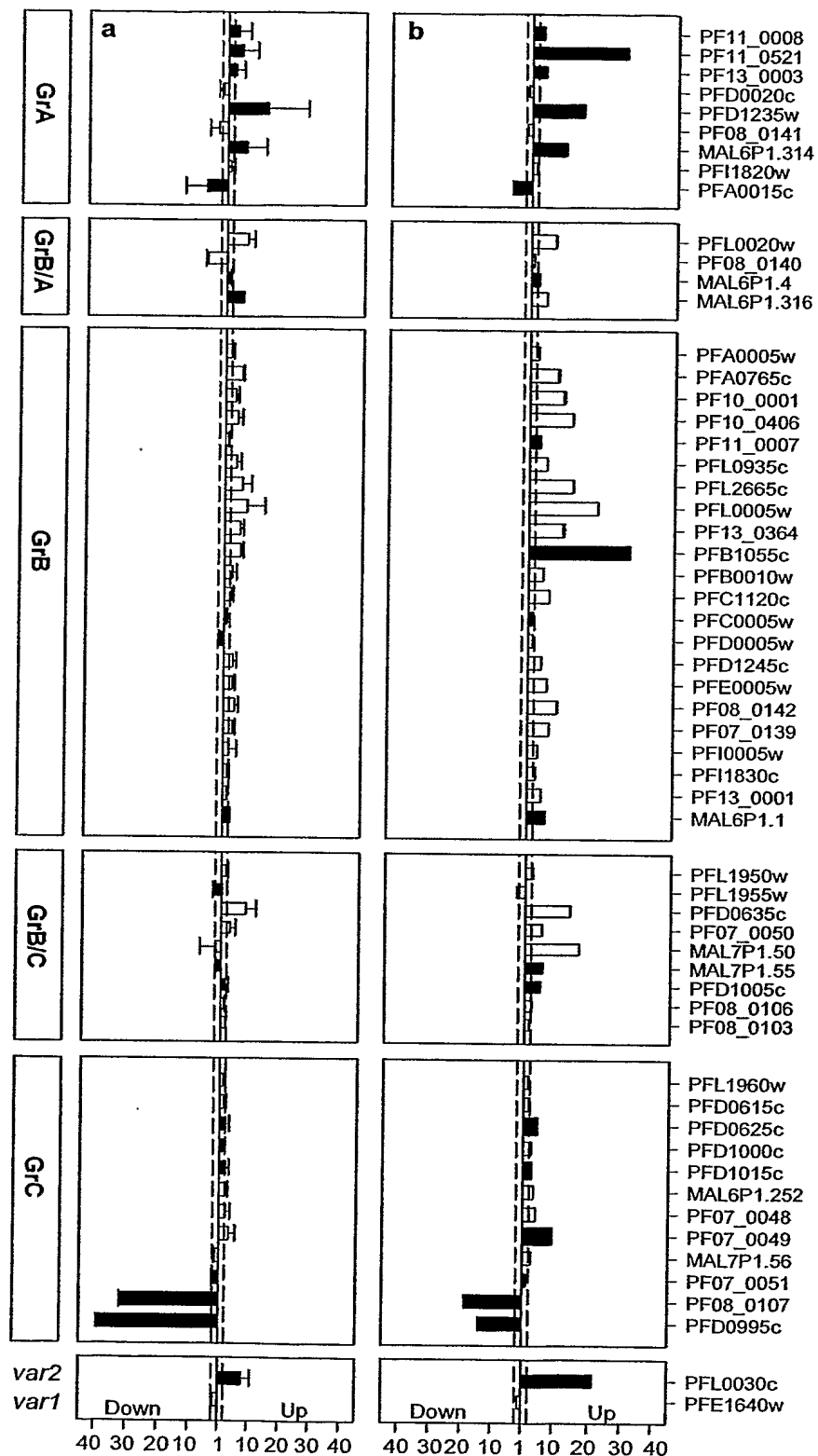
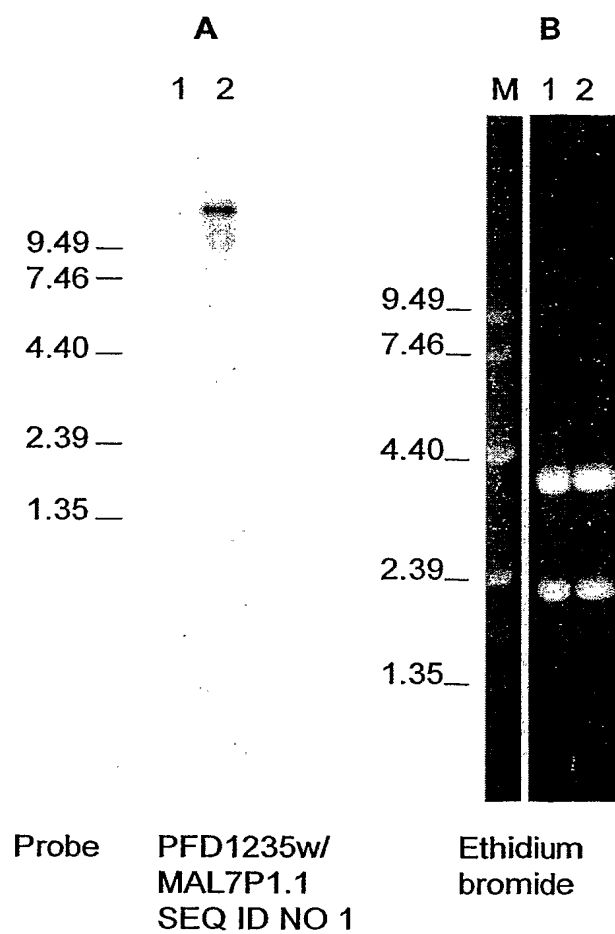


Fig. 14

17/25**Fig. 15**

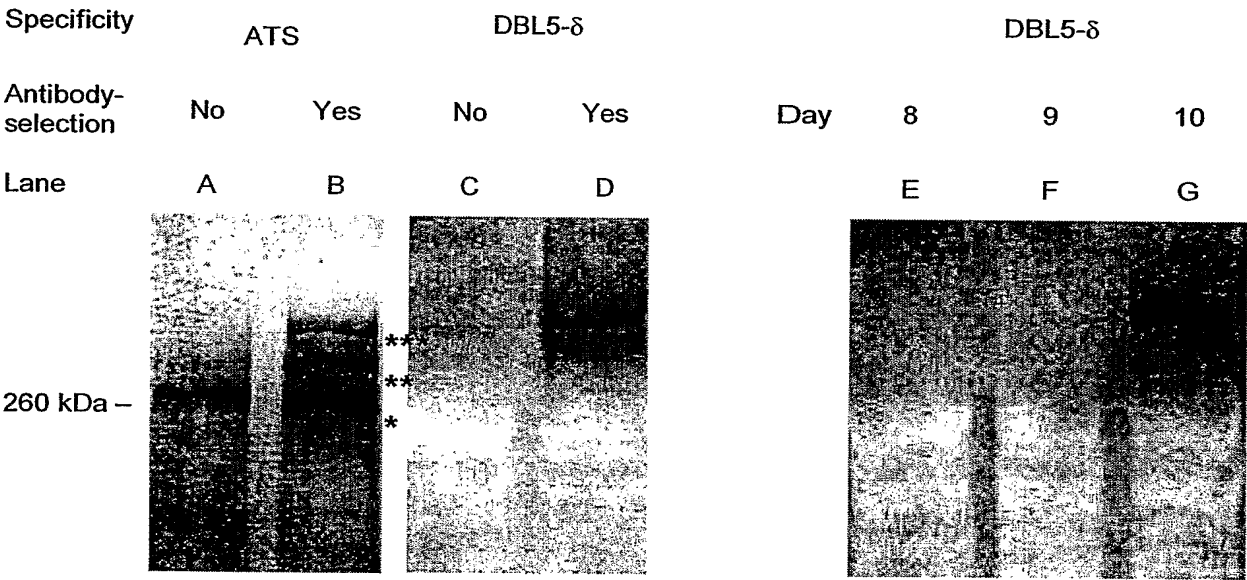


Fig. 16

19/25

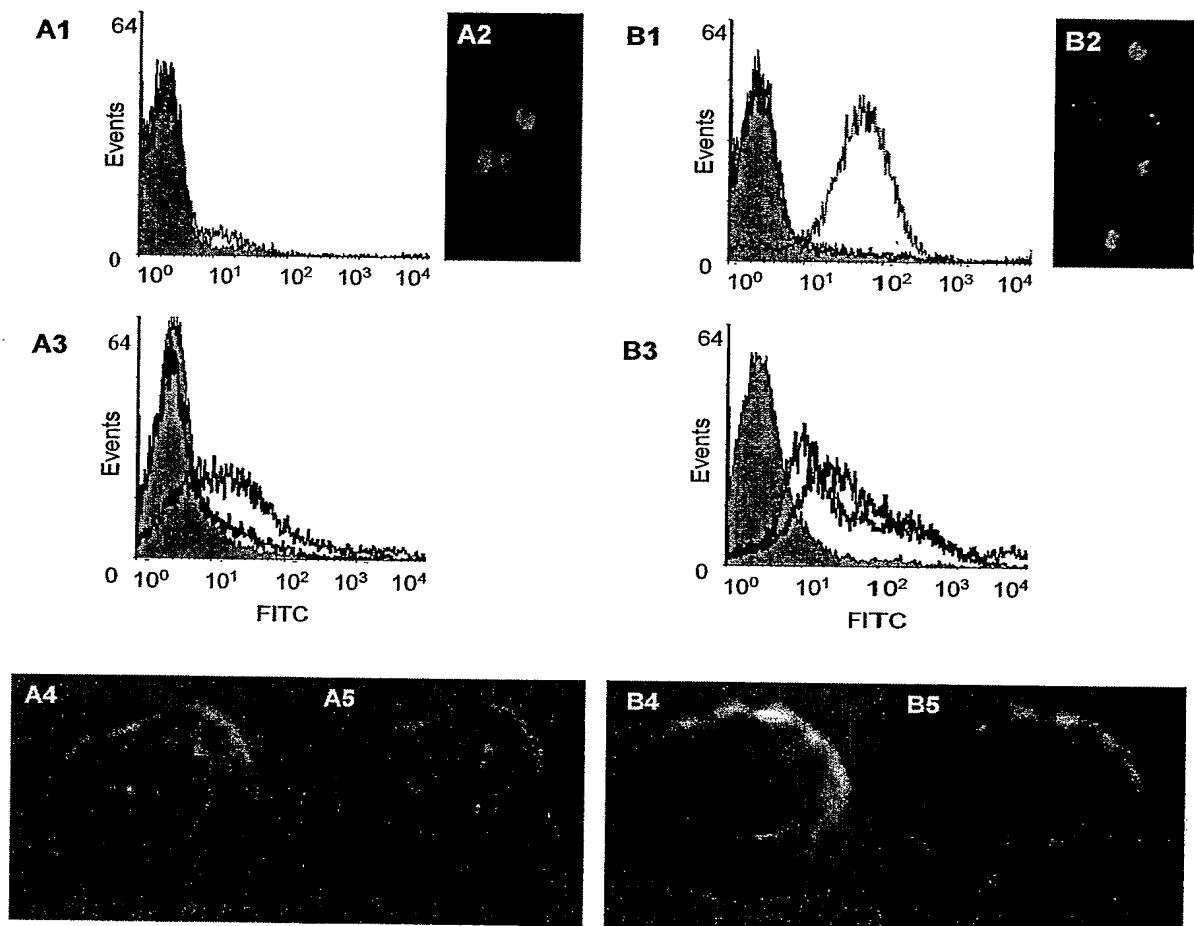


Fig. 17

20/25

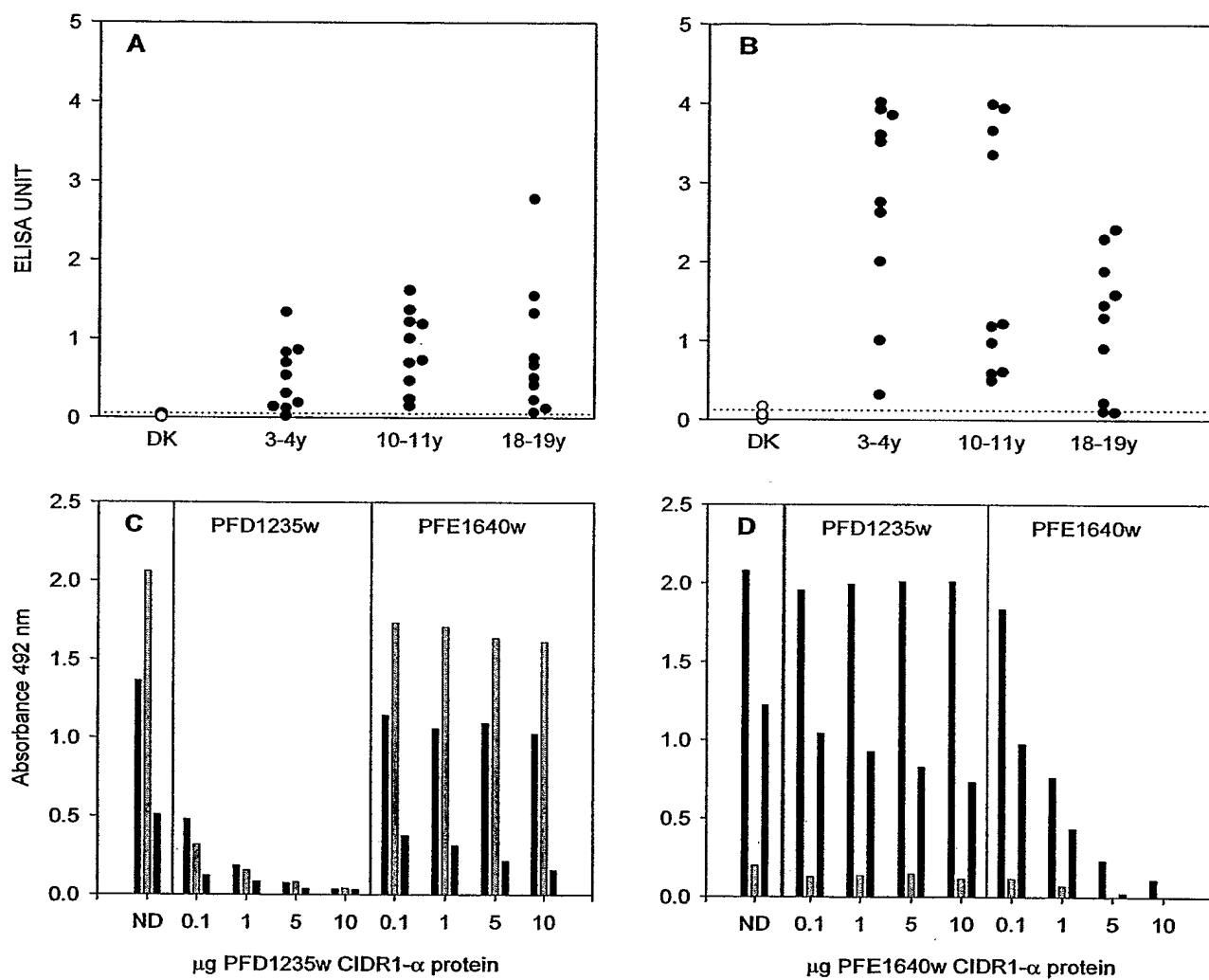


Fig. 18

21/25

```

*      20      *      40      *      60      *      80
BM021/1-76 : VVHNAEDRNPCLFSRseRFSNEGEAECSgdkIrdNge4sagGACAPYRRRyICDYNLHHINENNIRNTHDLLGN6LVMA4 : 81
BM048/1-76 : VVHNAEDRNPCLFSRseRFSNEGEAECSgdkIrdNge4sagGACAPYRRRyICDYNLHHINENNIRNTHDLLGN6LVMA4 : 81
PFD1235w/1 : VVHNAEDRNPCLFSRseRFSNEGEAECSgdkIrdNge4sagGACAPYRRRyICDYNLHHINENNIRNTHDLLGN6LVMA4 : 79

*      100      *      120      *      140      *      160
BM021/1-76 : FESEIVKSHSEYTGIGYKSGGCTSLARSFADIGDIRGNDLYLGINGMDRLNKLEIFKNIIDE TSTATRG KEALQA : 162
BM048/1-76 : FESEIVKSHSEYTGIGYKSGGCTSLARSFADIGDIRGNDLYLGINGMDRLNKLEIFKNIIDE TSTATRG KEALQA : 162
PFD1235w/1 : FESEIVKSHSEYTGIGYKSGGCTSLARSFADIGDIRGNDLYLGINGMDRLNKLEIFKNIIDE TSTATRG KEALQA : 157
SEGESIVKSHSEYTGIGYKSGGCTSLARSFADIGDIRGNDLYLGINGMDRLNKLEIFKNIIDE TSTATRG KEALQA : 157

*      180      *      200      *      220      *      240
BM021/1-76 : RYQHDAp 1YYqLREdWwtaNRhtVVKALTCsAPRDAQYFIKSSVRDQTFsNDYCGHGEHEVLtNLdYVPQFLRWFEES : 242
BM048/1-76 : RYQHDAp 1YYqLREdWwtaNRhtVVKALTCsAPRDAQYFIKSSVRDQTFsNDYCGHGEHEVLtNLdYVPQFLRWFEES : 242
PFD1235w/1 : RYQHDAp 1YYqLREdWwtaNRhtVVKALTCsAPRDAQYFIKSSVRDQTFsNDYCGHGEHEVLtNLdYVPQFLRWFEES : 238

*      260      *      280      *      300      *      320
BM021/1-76 : EFCRIKKIKLKNVKdACRDD3KaLYCgrNGYDCTKTnRN enLprgsKCTnCwaKcN6YEsWLnNqQeEfKkQKKeKyeKEI : 322
BM048/1-76 : EFCRIKKIKLKNVKdACRDD3KaLYCgrNGYDCTKTnRN enLprgsKCTnCwaKcN6YEsWLnNqQeEfKkQKKeKyeKEI : 322
PFD1235w/1 : EFCRIKKIKLKNVKdACRDD3KaLYCgrNGYDCTKTnRN enLprgsKCTnCwaKcN6YEsWLnNqQeEfKkQKKeKyeKEI : 319

*      340      *      360      *      380      *      400
BM021/1-76 : LKKNKNEKISGSHINNKYEDFKELEKK CANNHLKLLNEGKYNKKEKEE EMDFTNI EGTfYRSKCEVCF : 401
BM048/1-76 : LKKNKNEKISGSHINNKYEDFKELEKK CANNHLKLLNEGKYNKKEKEE EMDFTNI EGTfYRSKCEVCF : 401
PFD1235w/1 : LKKNKNEKISGSHINNKYEDFKELEKK CANNHLKLLNEGKYNKKEKEE EMDFTNI EGTfYRSKCEVCF : 398

*      420      *      440      *      460      *      480
BM021/1-76 : CGV2CrnTCTPKKKeYPCeInEaYiPpkDatpiDI3VLY3GDE2GDItkKLseFCs1eN4ENgENY2iWQCYYKnSDIN : 482
BM048/1-76 : CGV2CrnTCTPKKKeYPCeInEaYiPpkDatpiDI3VLY3GDE2GDItkKLseFCs1eN4ENgENY2iWQCYYKnSDIN : 482
PFD1235w/1 : CGV2CrnTCTPKKKeYPCeInEaYiPpkDatpiDI3VLY3GDE2GDItkKLseFCs1eN4ENgENY2iWQCYYKnSDIN : 478

*      500      *      520      *      540      *      560
BM021/1-76 : KCKMTPSSHKVPKHGYIMSF5AFFDLWVKNLLID3INWKNELTNCINNNTVTDCKNDCNTNCKCFENWAKTKENEWKKVKT : 563
BM048/1-76 : KCKMTPSSHKVPKHGYIMSF5AFFDLWVKNLLID3INWKNELTNCINNNTVTDCKNDCNTNCKCFENWAKTKENEWKKVKT : 563
PFD1235w/1 : KCKMTPSSHKVPKHGYIMSF5AFFDLWVKNLLID3INWKNELTNCINNNTVTDCKNDCNTNCKCFENWAKTKENEWKKVKT : 559

*      580      *      600      *      620      *      640
BM021/1-76 : IYKNENGNTNNYKKNL11FkGYFFHVMKE6NKEaKwNKLME1LKEKIDSSNLKNGTKDSEGAIKVLFdHLKDIAERCIDN : 644
BM048/1-76 : IYKNENGNTNNYKKNL11FkGYFFHVMKE6NKEaKwNKLME1LKEKIDSSNLKNGTKDSEGAIKVLFdHLKDIAERCIDN : 644
PFD1235w/1 : IYKNENGNTNNYKKNL11FkGYFFHVMKE6NKEaKwNKLME1LKEKIDSSNLKNGTKDSEGAIKVLFdHLKDIAERCIDN : 640

*      660      *      680      *      700      *      720
BM021/1-76 : NSNeSCdvSkD3KTNPcsetrGSKPTKSVKQLAEHMQQKAQKLLGTRGGESnLKGDAtrGTYNLGGQNTLNIGDICKITKN : 725
BM048/1-76 : NSNeSCdvSkD3KTNPcsetrGSKPTKSVKQLAEHMQQKAQKLLGTRGGESnLKGDAtrGTYNLGGQNTLNIGDICKITKN : 725
PFD1235w/1 : NSNeSCdvSkD3KTNPcsetrGSKPTKSVKQLAEHMQQKAQKLLGTRGGESnLKGDAtrGTYNLGGQNTLNIGDICKITKN : 721

*      740      *      760
BM021/1-76 : ITNDSRNGEPCGTGKDKYNGFRLNIGTPTWNIQAKKK : 764
BM048/1-76 : ITNDSRNGEPCGTGKDKYNGFRLNIGTPTWNIQAKKK : 764
PFD1235w/1 : ITNDSRNGEPCGTGKDKYNGFRLNIGTPTWNIQAKKK : 760

```

Fig. 19

22 / 25

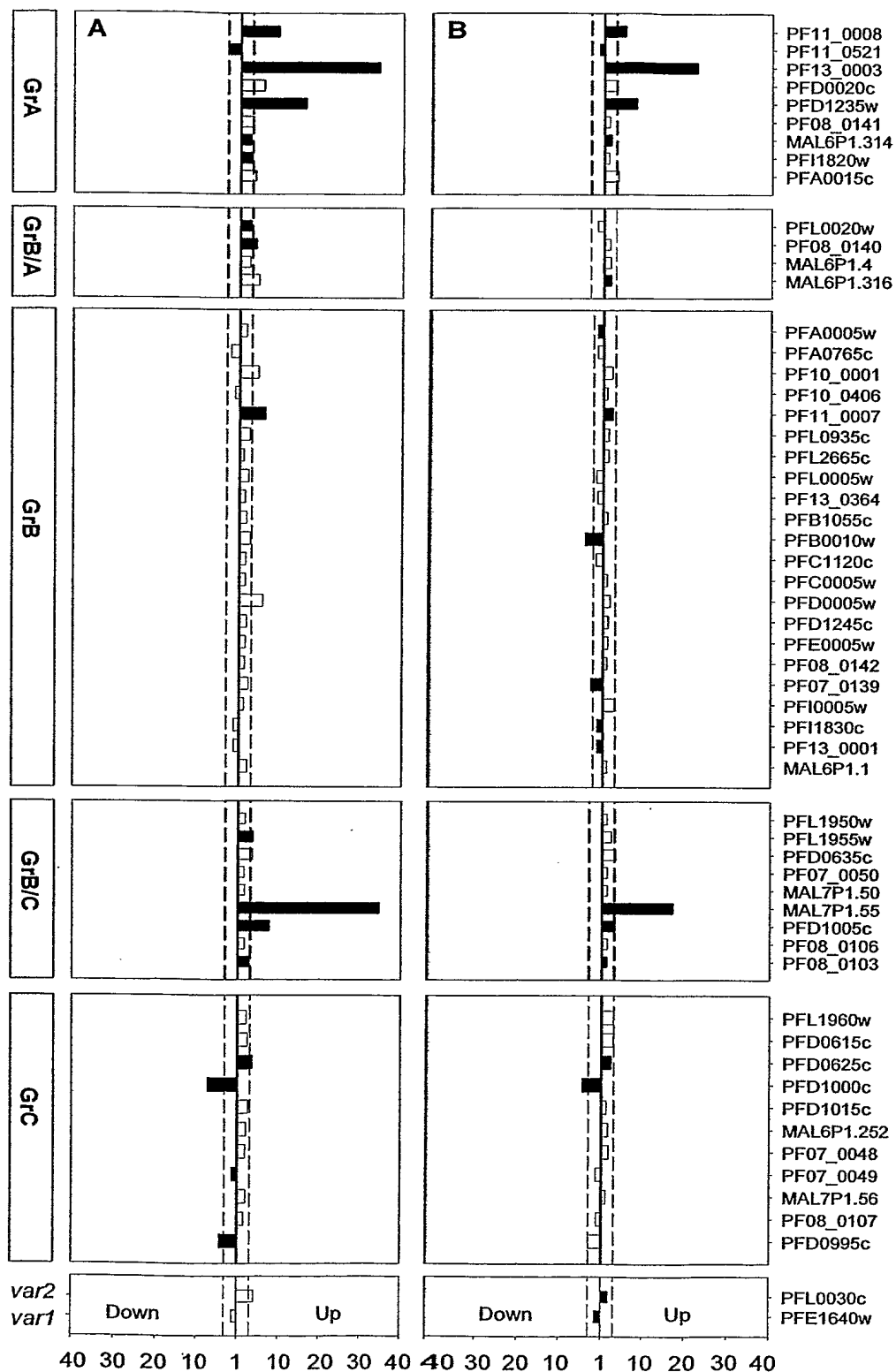


Fig. 20

23/25

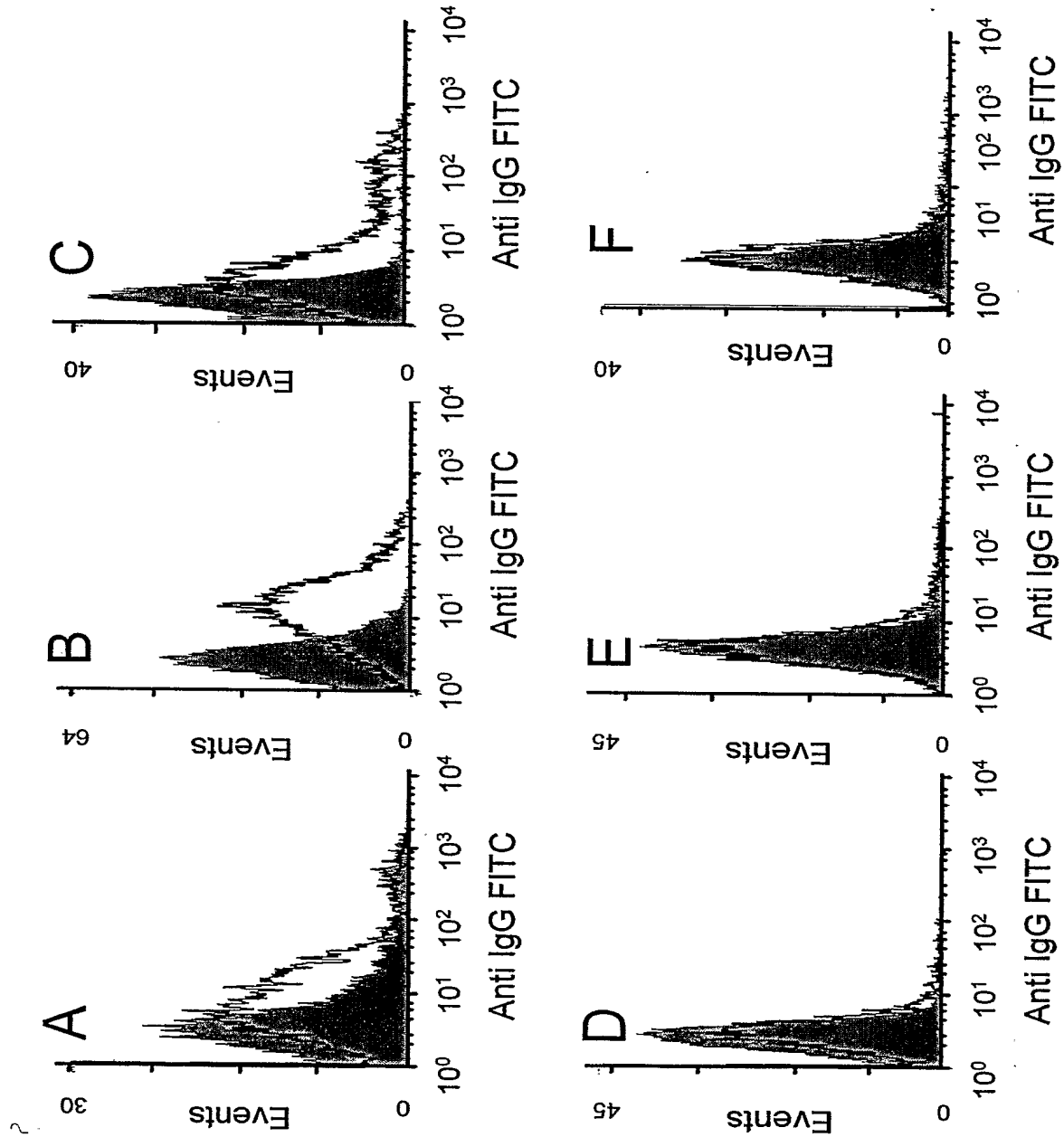


Fig. 21

24/25

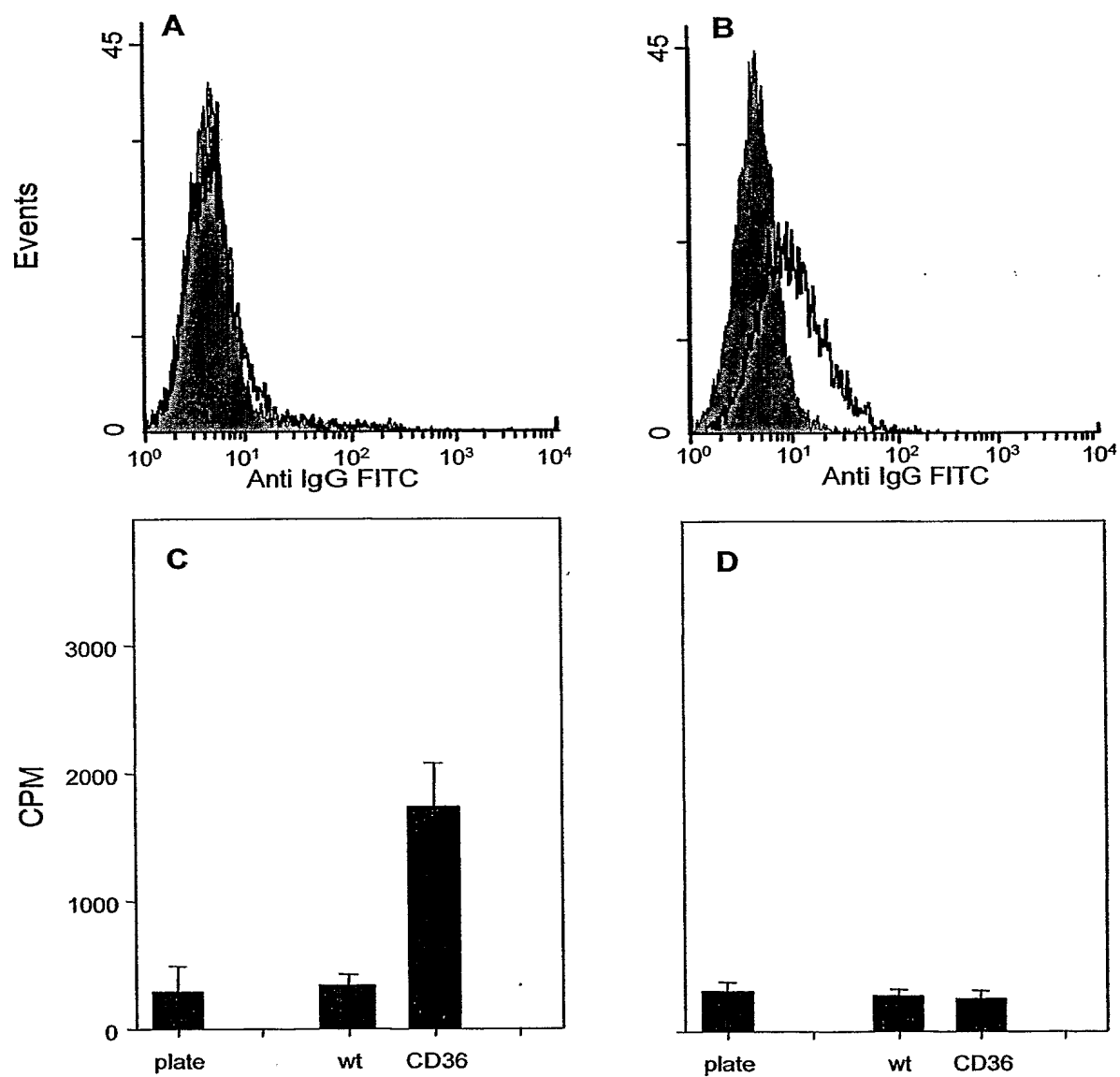


Fig. 22

25/25

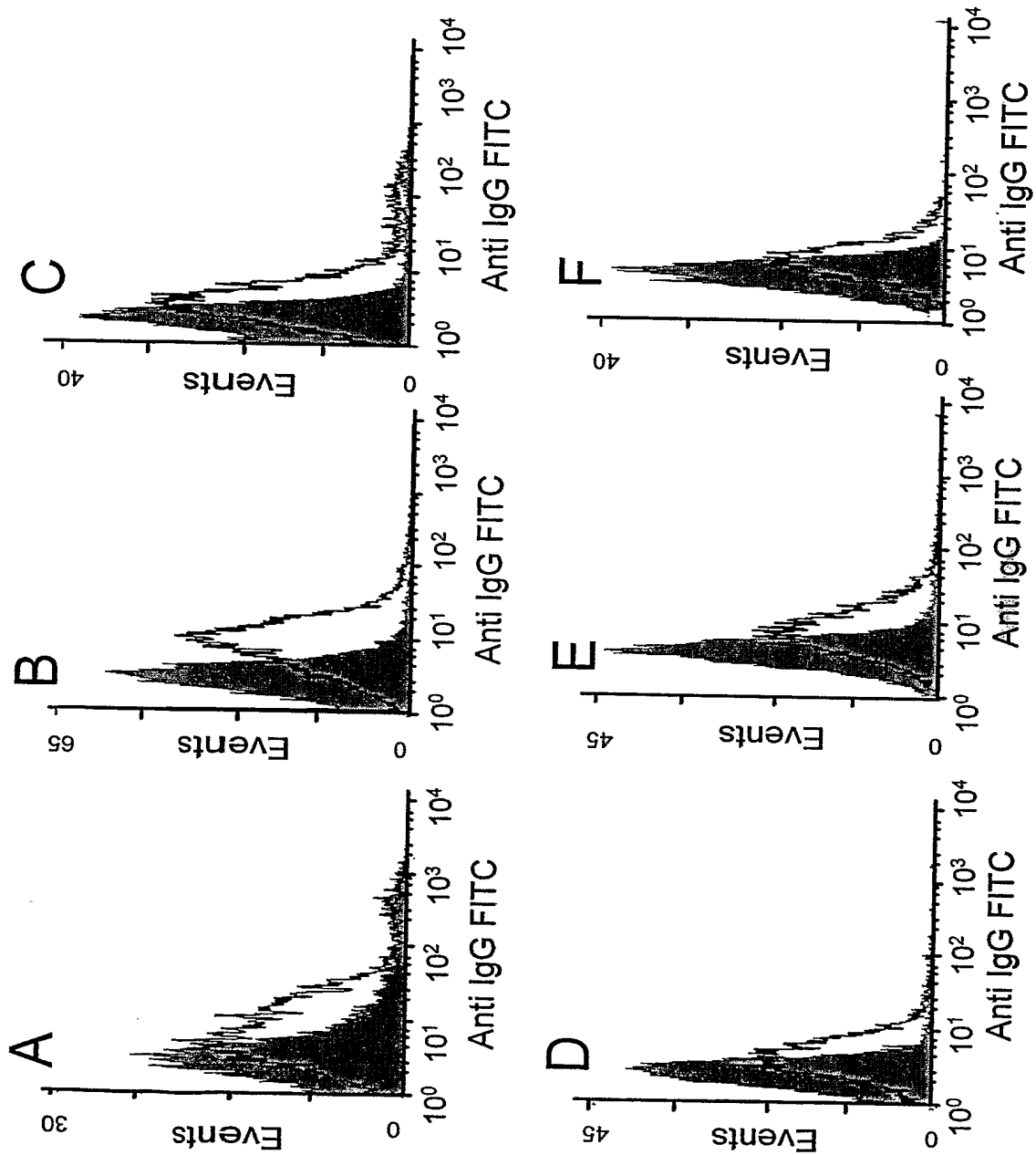


Fig. 23